The Erasmus Wilson Lectures

ON THE

PATHOLOGY OF THE LYMPHADENOID STRUCTURES

2.

Delivered at the Royal College of Surgeons of England on
March 1st, 3rd, and 5th, 1897

BY

W. G. SPENCER, M.S., M.B. LOND., F.R.C.S. ENG.,

SURGEON TO OUT-PATIENTS AND THROAT DEPARTMENT, WESTMINSTER HOSPITAL, AND
LECTURER ON PHYSIOLOGY AT WESTMINSTER HOSPITAL MEDICAL SCHOOL.

ROYAL COLLEGE OF SURGEONS OF ENGLAND
-8 APR 97
LIBRARY

Reprinted from THE LANCET, March 6, 13, and 20, 1897.

The Erasmus Wilson Lectures

ON THE

PATHOLOGY OF THE LYMPHADENOID STRUCTURES.[1]

LECTURE I.

Delivered on March 1st.

GENTLEMEN,—The organs composed of lymphadenoid tissue are the bone marrow, the spleen, the thymus, and the glands and follicles in the mucous membrane of the alimentary and respiratory canals, but new formations may also appear in connective tissue where normally there is little sign of it. Lymphadenoid tissue is a specialised kind of white fibrous tissue in the meshwork of which free cells collect. These cells produce blood corpuscles and also retain the fundamental digestive powers of unicellular organisms. In consequence of the situations in which lymphadenoid tissue is developed waste products of tissue change are prevented from entering the circulation until they have been rendered harmless, and thus its function of protecting the body from waste products—metabolites—of normal origin is capable of extension and is thus able to offer some resistance to the spread of disease, either by counteracting the poisonous substance resulting from diseased tissues or by actually destroying the germs of disease themselves. The pathological conditions to which lymphadenoid tissue is itself subject arise in the course of the performance of the protective functions. Being excited to over action lymphadenoid tissue becomes the starting point of new growth, or it is replaced by scar tissue as a consequence of inflammation, so that the production of the red and white blood corpuscles is disturbed and the rest of the body thereby affected.

---

[1] These lectures were illustrated by specimens from the Anatomical and Pathological Museums of the Royal College of Surgeons of England and of the Westminster Hospital.

THE ORIGIN OF LYMPHADENOID TISSUE.

Lymphadenoid tissue is produced—(1) as lymphatic glands around the plexus of lymphatic trunks where they join in the axilla, groin, &c. ; (2) around epithelial masses and glands, as the tonsils, thymus, salivary glands, and intestinal follicles ; or (3) in the wall and sheath of the small bloodvessels in the spleen and bone marrow, favoured by the slow rate of the circulation. Fibrous connective tissue is changed into retiform tissue by a splitting up of its individual fibres, and into the meshwork so formed white cells emigrate from the capillary bloodvessels, and there, by multiplying, establish germinating centres. Fine capillaries permeate these germinating masses, but not so the lymphatics. The latter begin in a sinus outside the follicle, into which the young cells pass as they are pushed out from the centre by still newer formations.

Lymphadenoid tissue, like connective tissue generally, is prone to vary. An increase of the blood flow accelerates the multiplication of cells and so causes an overgrowth ; a diminution in the blood-supply promotes a fatty metamorphosis, from which a renewal of lymphadenoid tissue may at any time take place—red marrow replaces the yellow, lumps of apparent fat develop again into glands, or minute glands consisting of only a single follicle can as the result of irritation become compound glands.

THE FUNCTIONS OF LYMPHADENOID TISSUE.

A.—The Formation and Destruction of Red Corpuscles.

The red corpuscle, although varying in type among vertebrates, is uniform in each species after embryonic life and during health. Its sole function is to carry oxygen, and in no other way can this action be carried out ; the imperfect red corpuscles which gain access to the blood in disease appear incapable of properly doing this work. Further points of difference between it and the white corpuscle are that the red are never produced in excess, neither do they take part in new formations of any kind, nor have they any digestive powers, nor do they produce a protective secretion.

1. Red blood corpuscles are first formed from colourless cells outside the bloodvessels. They are first seen in the area vasculosa of the chick—i.e., outside the embryo itself, arising from cells of the mesoblast, previously colourless, which develop hæmoglobin in their protoplasm. There is therefore no *a priori* objection to the development at later periods also of young red cells or erythroblasts from colourless cells since the erythroblasts have in the beginning an origin in common with the young white corpuscles or

leucoblasts (Neumann). On the other hand it is held that the erythroblasts of the embryo form a distinct order of cells which remain throughout life the only source of the red corpuscle (Bizzozero). The cells which form the blood islands begin to show hæmoglobin before the bloodvessel has developed around them, so that the first formation of red cells may be called extra-vascular. Later there is a very similar appearance in all the blood-forming organs, but it has not yet been settled whether the groups of erythroblasts undergoing division are placed in the lumen of the capillary or within a diverticulum of the capillary, whether they form the capillary wall itself at the point, or whether they are in the tissue outside separated from the blood stream by a layer of endothelium.

2. Red corpuscles after being formed in connective tissues are produced in later embryonic life in special organs. Erythroblasts are met with widely in the connective tissue and especially in the case of the mammalian embryo, in the walls of the umbilical vesicle, intestines, and bladder, as well as in the subcutaneous tissue (Saxer).[2] As the lymphadenoid tissues develop erythroblasts gradually disappear from the blood and only re-appear under abnormal circumstances. They also gradually disappear from the walls of the intestines and umbilical vesicle and their production becomes concentrated in the liver. The liver of the mammalian embryo takes a very important part in blood formation; it is relatively a very large organ, in the capillaries of which erythroblasts and leucoblasts are seen undergoing mitosis side by side, and according to Kostanecki[3] they have an origin in common. In late embryonic life this formation in the liver diminishes and ceases before birth. Erythroblasts are also seen during the latter part of embryonic life in the hilum and follicles of lymphatic glands, in the spleen, and in the thymus.

3. After birth the formation of red corpuscles becomes gradually confined to the red marrow in the higher mammals and man, although in lower vertebrates lymphadenoid tissue, especially the spleen, retains this function throughout life. The red marrow of birds forms a good material for demonstrating the various structures (Muir and Drummond).[4] In the capillary lumen are seen fully developed red corpuscles, in the wall are young red cells or erythroblasts which, although they project into the lumen, are fixed and show signs of mitosis; in the tissue around the capillary are the white cells rapidly dividing and passing towards the capillary channel.

---

[2] Saxer: Centralblatt für Allgemeine Pathologie und Pathologische Anatomie, 1896, vol. vii., p. 421.

[3] Kostanecki: Anatomische Hefte, 1892, Band i.

[4] Muir and Drummond: Journal of Anatomy and Physiology, 1894, vol. xxviii., p. 125.

On the whole it would appear most probable that the red corpuscles originate after birth from the small white cells of the marrow, and that the erythroblasts represent an intermediary stage. The alternative view is that the erythroblasts seen in the red marrow of the adult are a special class of cells directly derived from those found in the embryo.

Anæmia and regeneration of the red corpuscles.—There is an entire absence of clinical and experimental evidence as to the production of red corpuscles in excess. At any rate there is nothing comparable to leucocytosis and leucocythæmia in the case of the red corpuscle. A diminution in the rate of production of the red corpuscles seems to be the cause of the anæmia which occurs in women leading an indoor life, in those who have an insufficient supply of albuminous food, as well as in old age. And clinical experience definitely shows that the recovery up to the normal rate of production is a slow process. Anæmia can be produced experimentally in one of two ways, either by removing a considerable amount of blood or by the introduction into the circulation of some material which will increase the rate at which the red corpuscles are destroyed.

The regeneration of the blood after loss is seen when a considerable amount of blood has been taken from an animal by repeated venesections; the marrow then exhibits an increased mitosis both of colourless and coloured cells and becomes more red, the spleen swells up and erythroblasts showing mitosis are found within it, and similar immature nucleated red corpuscles are seen free in the blood stream (Freiberg[5] also Autokonenko[6]). According to Grünberg[7] erythroblasts are also to be seen in lymph glands, the intestinal follicles and tonsils, more especially when the spleen had been removed before the venesections were made. The lymph glands most affected were those of the mesentery, axilla, groin, and neck, which appeared to the naked eye enlarged and reddened. The lymphatics leading from the enlarged glands were filled with true red corpuscles, nucleated ones, and white cells. The germinating follicles of the lymph glands were exceedingly rich in leucoblasts undergoing mitosis. He speaks of the erythroblasts and red corpuscles as being in the lymphatic gland sinus, but only of leucoblasts within the stroma of the gland itself—under the foregoing condition no erythroblasts and red corpuscles were seen in the thymus (Braunschweig[8]). Venesection appears therefore to excite the leucoblasts to more rapid production, and there is a return to the embryonic state as regards the production of the red corpuscles. The alternative explanation of the appearances seen after great loss of blood is that the production of erythroblasts in the marrow is stimulated and that some are detached and carried to the spleen and lymph glands, where they continue to divide until the loss is restored, when the formation of red cells is again confined to the red marrow (Zenoni[9]; also Disse[10]).

---

[5] Freiberg: Inaugural Dissertation, Dorpat, 1892. Centralblatt für Pathologie, &c., 1893, Band iv., S. 460.

[6] Autokonenko: Archives des Sciences Biologiques, 1893, vol. ii., p. 516.

[7] Grünberg: Dissertation, Dorpat, 1891; quoted by Disse, vide infra.

[8] Braunschweig: Ibid.

Destruction of red cells in connexion with the spleen and also in the liver is attended by an increased production of leucocytes, and it is the increased production of these cells which appears to be the cause of the hæmolysis. According to Hunter an increased destruction of red cells takes place during digestion in the spleen at a time when there is an increased production of leucocytes by that organ and by the gastro-intestinal wall. Hæmolysis in a greater degree can be brought about by acting either directly upon the blood or indirectly through the spleen and gastro-intestinal lymphadenoid tissue by injecting such a drug as toluylendiamin. The spleen enlarges several fold owing to engorgement with venous blood, iron containing pigments collect in the spleen and liver, and there is an increased secretion of bile, some of which may be absorbed and produce jaundice. Red corpuscles in various stages of degeneration are to be seen in the spleen. When, however, the spleen is first of all removed much larger doses of the drug are required to produce the hæmolysis which then takes place through the lymphadenoid tissue of the intestinal wall. The toluylendiamin at the same time markedly increases the number of white cells in the blood, and the explanation of its action is that it first excites leucocytosis, especially in the spleen, but also in the intestinal wall, and that it is the leucocytosis which is the cause of the hæmolysis. When drugs are injected which destroy the blood directly the removal of the spleen causes no alteration in the result (Hunter).[11] The anæmia, therefore, which is seen in the diseases of the lymphadenoid structures appears to originate in an excessive production of white cells, which hurry on and push out into the circulation whilst immature the red corpuscles in such a state that they cannot act fully as normal oxygen carriers and are liable to be destroyed.

B.—The White Blood Corpuscles.

Leucocytes are all alike throughout the vertebrata, although in many species they can be divided into several kinds. They seem to be distinct from the fixed cells of the tissues, but this point is by no means definitely settled. White blood corpuscles, small marrow cells, the wandering cells, the lymphocytes as well as the free cells in the mouth, intestines, and bronchi, all originate from the cells in the meshes of lymphadenoid tissue. They are practically protozoa which can be kept alive outside the body and so be studied under the microscope. In the course of lymphadenoid disease the leucocytes, except for a temporary occasional diminution to a slight degree, are increased, sometimes, indeed, ten or twenty times, due to the abnormal excitation of lymphadenoid tissue.

---

[9] Zenoni: Virchow's Archiv, 1895, Band cxxxix., p. 185.

[10] Disse: Ergebnisse der Anatomie und Entwickelungsgeschichte von Merkel und Bonnet, 1895, Band v., s. 30.

[11] Hunter: Physiology and Pathology of Blood Destruction, THE LANCET, Nov. 26th, Dec. 3rd, 10th, and 17th, 1892, pp. 1259, 1318, 1371. The Pathology of Jaundice, Journal of Pathology and Bacteriology, 1895, p. 259.

1. In whatever situation these cells are found they exert a protective function due either to their secretion or to their ingesting and digesting powers. In the course of normal digestion an excess of leucocytes appears in the blood, and at the same time there is a marked enlargement of the spleen from which the cells are derived. This normal leucocytosis seems to have as its object the removal of some harmful products of digestion. In a less regular way some leucocytosis may occur during pregnancy and in the newborn infant.

2. Leucocytes play an active part in the removal of embryonic structures. Metchnikoff has described the removal by this means of the tadpole's tail, and Kowalewski that of the organs of the larva to make way for those of the imago. The epithelial structure of which the thymus is at first composed disappears before the invasion of the lympadenoid tissues.

3. Free leucocytes in the mouth derived from the tonsils, in the intestine from the solitary and agminated follicles, and also similar cells in the bronchi, all have a deterrent action upon the growth of micro-organisms in these cavities.

4. As to inflammatory reaction, upon the inoculation of disease germs into an animal capable of offering a resistance to their attack, a local inflammatory reaction takes place, consisting of an increased circulation, but more especially of a rapid collection of leucocytes, and by multiplying rapidly these cells and their secretion may prevent the spread of the disease. If the organisms succeed in developing, the lymphadenoid tissues placed on the line of the lymphatics running from the site of innoculation may present a second line of defence against the invasion of the body There is an increased circulation through the gland and rapid mitosis, so that more cells are produced, the gland appearing swollen and redder than usual. In it bacilli such as those of tubercle may lodge and be there digested If, however, the bacilli gain the circulation they may be destroyed in one of two ways. They may be destroyed in the blood stream, an increased production of leucocytes being excited in all the lymphadenoid organs by the destruction of cells, or the organism may lodge in the spleen, as in anthrax and relapsing

fever, and be there included by the splenic cells. If the animal, however, presents no great resistance, the micro-organisms quickly develop, whilst but few leucocytes gather round them. Even if they are checked for a time at the lymphatic glands, the organism succeeds in growing through and gains the circulation, which before death contains numbers free in the plasma, not included either in the white blood corpuscles or in the spleen cells.

The destruction of diseased germs may be due either to the cell ingesting them whilst still alive or by the secretions or products of the cell killing the organisms, and after they are dead the white cells swallow and digest them. It is generally agreed that white cells swallow and digest dead bacilli in the same way that unicellular organisms take in their food, a vesicle containing a peptic secretion is developed, the food material is dissolved, and the débris evacuated. But there has been much opposition to Metchnikoff's view that bacilli are ingested alive.

Wooldridge was the first to show that the secretions and cell products of lymphadenoid tissue can hinder or prevent the development of micro-organisms. In some experiments which I had the opportunity of watching he demonstrated that rabbits could be made immune to the inoculation of anthrax bacilli by injecting material derived from the thymus gland. Hankin and others have since then developed the large subject connected with the defensive proteids or alexins which are formed in connexion with the white cells. One method of experiment to show the power of the fluids in a resisting animal is to wrap the bacteria up so that no cells can come in contact with them, and in this way the most resisting anthrax spores may be destroyed. According to Kanthack and Hardy[12] the granules seen in some leucocytes, such as those which stain with eosin, represent the secretion of the cell.

Leucocytosis.—The production of leucocytes in excess of the normal can be brought about by the injection of the products of animal and of vegetable cells. Of animal products there are especially those derived from nuclei such as nucleo-albumin, nuclein, nucleic acid, uric acid, also other nitrogenous products such as urea, peptone, albumose, spermin, and bacterial products, pyocyanin tuberculin; among vegetable materials are curara, papayotin, abrin, pilocarpin, terebinthin, and cinnamic acid. These either excite lymphadenoid tissue directly or do so indirectly by destroying cells. Many diseases cause a considerable leucocytosis probably in the same way; it is met with in cancerous cachexia, in the stage before death, after hæmorrhage, in inflammation of the serous membranes, and in pneumonia. This leucocytosis when it occurs in the general diseases of lymphadenoid tissue is termed leucocythæmia or leukæmia. A slight degree of leucocytosis may exert a favourable influence. Löwy and Richter[13] found that rabbits required much larger doses of such virulent materials as cultures of diphtheria, chicken cholera, pig typhoid organisms, or pneumococci, in order to affect them after a certain degree of leucocytosis had previously been produced whether by the injection of spermin, pilocarpin, &c., or by the production of hyperpyrexia by puncture of the corpus striatum. According to Pawlowsky[14] rabbits in which a local leucocytosis was produced at the site of the inoculation of an anthrax culture by the injection of papayotin or abrin recovered, whereas the control animals similarly inoculated, but in which no leucocytosis was afterwards produced, died. An excessive leucocytosis or leucocythæmia is unfavourable, not only by destroying red cells and disturbing the production as already pointed out, but by promoting an excessive destruction of white ones also. This continued cell destruction keeps up the excessive production by the lymphadenoid tissue and liberates from the nuclei of the cells proteids which set up intra-vascular coagulation, and hence the thromboses, ulcerations, and hæmorrhages which accompany leucocythæmia. It is the mature white corpuscles probably which have the chief protective power; and so the young white cells hurried into the blood in leucocythæmia before they have developed are unable to act as protecting agents, and tend quickly to break down.

---

[12] Kanthack and Hardy: Philosophical Transactions, 1894, vol. clxxxv., p. 279.

We have thus traced back the anæmia and leucocytosis or leucocythæmia seen in connexion with the diseases of lymphadenoid tissue to the same cause—an excess of cell-products which excite the divisions of the leucoblasts, in consequence of which unripe red cells are hurried into the circulation from the bone-marrow, and, being inefficient as oxygen carriers, are soon included and destroyed in the spleen; at the same time the immature white cells which get into the circulation cannot fulfil their protective functions and may soon liberate substances which cause intravascular coagulation.

THE SPLEEN.

The spleen is an important blood-forming organ in amphibia and fish, and also in the mammalian embryo, but no proliferating red cells are to be seen in the healthy adult spleen of man. The centre of the Malpighian bodies is the site of the active germination of white cells, which pass to the periphery of the follicle and so get into the lymphatics.

---

[13] Löwy und Richter: Centralblatt für Wissenschaftliche Medicin, 1895, S. 445.

[14] Pawlowsky: Atti dell' XI. Congresso Medico, Roma, 1894, vol. ii., Patologia generale, 165.

After leaving the spleen they pass through glands about the tail of the pancreas and through the cœliac glands into the thoracic duct. The cells lining the spaces of the spleen pulp, through which the blood slowly flows, englobe and destroy red corpuscles and other foreign and harmful material. This function is especially active during digestion when the organ swells. The inherent rhythmical contractility residing in the unstriped muscle of the capsule and trabeculæ of the spleen favours the return of venous blood from the pulp spaces, especially after these have become distended during digestion. This rhythmical contractility has been not only the subject of experiment in animals, but has been observed during operations upon man. The spleen has been seen to contract under the eye when the return of venous blood had been hindered previously by its displacement. The spleen when prolapsed into a wound, so that the efferent veins are compressed, quickly becomes enormously swollen.

The effect of removal of the spleen.—Complete splenectomy produces a temporary anæmia and enlargement of lymph glands, but neither condition is well marked. They occur both after experimental splenectomy in animals and also in the human subject when a spleen has been removed which had up to a short time before been healthy—e.g., when the spleen has been removed for injury or on account of a twisted pedicle (Ballance).[15] No change follows upon the removal of a diseased spleen, either in the blood or in the lymph glands, for the functions of the spleen have already been assumed by the lymph glands, &c., before the operation. Some experimenters on animals have found them little affected by it. The existence of a spleniculus which hypertrophies when the spleen is removed may explain this absence of symptoms, or, owing to a small portion of the spleen being left on the proximal side of the ligature, the spleen may re-form (Laudenbach).[16] After partial resection, however, healing takes place simply by scar tissue without any hypertrophy.

The protective functions of the spleen.—The cells of the spleen pulp can stop and remove from the circulation abnormal blood corpuscles, pigment, and some forms of organisms. Large cells are seen enclosing red or white corpuscles, bacteria, &c. (cellules d'arrêt: Cæsaris Demel).[17] According to Metchnikoff[18] and Soudakewitch[19] the spirilla of relapsing fever multiply rapidly in the blood, but on reaching the spleen they are taken up and destroyed. If the cells become exhausted spirilla escape, and becoming again free in the blood rapidly increased again. Werigo [20] noted that anthrax bacilli injected into the ear vein of a rabbit reach the spleen and liver and are there included by cells. But soon free bacteria are found in the spaces of the spleen pulp, and then they multiply rapidly and cause the spleen to swell. During the last stages of the disease the bacteria escape into the general blood stream. There are other parasitic diseases—such as typhoid fever, diphtheria, and malaria—where the spleen appears also to play, in part at least, a protecting *rôle.* But, on the other hand, there are conditions in which it remains unaffected.

---

[15] Pitts and Ballance: Transactions of the Clinical Society, 1896, vol. xxix., p. 102. Also discussion by Ballance, Bland Sutton, &c., THE LANCET, Feb. 22nd, 1896.

[16] Laudenbach: Virchow's Archiv, 1895, Band cxli., S. 201.

[17] Cæsaris Demel: Archives Italiennes de Biologie, 1896, tome xxvi., p. 83.

[18] Metchnikoff: Virchow's Archiv, 1887, Band cix., S. 176.

[19] Soudakewitch: Annales de l'Institut Pasteur, 1891, tome v., p. 545.

The pathological changes in the spleen arise either in connexion with disturbances of its circulation or are due to inflammatory changes consequent upon the collection of morbid products in it. A diseased spleen affects the body generally either by producing leucocythæmia and anæmia or by acting as an abdominal tumour.

Circulatory disturbance.—Venous obstruction concurrent with obstruction to the portal circulation causes first an engorgement of the pulp, then a general increase of connective tissue which does not especially pick out the follicles. Embolism affects the spleen according to the vessel, whether a main vessel is affected or several small ones. In pyæmia the necrosis goes on to suppuration around the bacteria which have lodged there. Infarcts from thrombosis are a special feature of the spleen. They are met with in typhoid fever, malaria, and leucocythæmia owing to the coagulation produced by the breaking down of leucocytes. A wedge-shaped mass is formed abutting on the surface, which can thus be distinguished from other changes.

Inflammatory changes the result of infection.—The spleen is rarely affected by tubercle until the disease has become generalised. The bacilli have to pass through lymphatics and lymphatic glands into the blood stream before they can reach the spleen. The tubercles generally form in the sheath of the bloodvessels and in the Malpighian bodies. The Malpighian bodies appear as pale, firm masses which may easily be confounded with the changes due to lymphadenoma. Syphilis, especially when inherited, affects the spleen either directly in the form of gummata or by a general overgrowth of connective tissue or indirectly by starting amyloid disease. Amyloid disease may commence in a previously healthy spleen from some cause other than disease of lymphadenoid tissue, and by commencing in the follicles form the so-called "sago spleen," or it may be widely diffused around the vessels of the pulp, and give rise to a hyalin appearance on section which has been compared to bacon rind. Amyloid disease may also affect a spleen previously altered by malaria, tubercle, syphilis, &c.

---

[20] Werigo: Ibid., 1894, tome viii., p. 1.

The spleen in malaria.—In malaria the spleen is primarily affected by an increased vascularity, in connexion with which there is an inclusion by the cells of the pulp of the corpuscles which are degenerating owing to the parasites, and there is left behind much pigment. This increased vascularity may cause only a temporary swelling of the spleen, and the organ afterwards subsides. The more permanent enlargement is due to an increased connective tissue formation whether specially of the follicles or diffusely of the pulp. Infarcts also occur. The stopping function of the spleen may be so far successful that the patient ceases to suffer from malaria. Presumably in such a case the spleen has taken a prominent part in removing the parasites from the circulation. The spleen may not, however, subside after the cessation of the malaria, but remain an abdominal tumour, obstructing by its large size the abdominal circulation, and being in danger of causing at any time intra-peritoneal hæmorrhage either by the rupture of the tumour itself from some slight injury or often adhesions which have formed between the capsule and neighbouring structures. Such patients remain thin and anæmic, and an improvement in health may follow on splenectomy, always provided that the malaria has subsided and there is no leucocythæmia present. The improvement may be due simply to the removal of an abdominal tumour forming a mass of diseased tissue.

THE BONE MARROW.

Red and yellow marrow.—From the time when ossification commences in the previously non-vascular fœtal cartilage by an invasion of bloodvessels from the perichondrium there appear erythroblasts developing into red corpuscles, and at a later period leucoblasts, which form the small colourless cells. Wherever ossification is going on there is an active formation of red corpuscles; and not only in cartilage and membrane, but also in exceptional cases of ossification, such as those which occur late in life in the laryngeal and rib cartilages, Neumann found erythroblasts. The formation of the red corpuscles in the red marrow is a feature common to all vertebrates, and is only absent in those fish whose cartilage persists throughout life as solid rods. In adult mammals it is the sole manufactory for the red corpuscles. The red marrow, however, gradually disappears from the bones of the extremities, being last of all found in the cancellous tissue of the upper end of the humerus and femur. It is present in the flat bones, especially in those of the vertebræ and skull, although even in the flat bones yellow marrow takes the place of much of the red late in life. The yellow marrow which fills the long bones of the adult must not be regarded as identical with the fat of connective tissue. It must be compared with the fatty masses which replace the thymus and lymphatic glands, for under certain circumstances the yellow again changes to red. It is also asserted that the administration of yellow marrow has had a beneficial effect in anæmia by promoting the production of red corpuscles, a result which cannot be attributed to simple fat. Marquis[21] has described the marrow in the long bones of the frog which is red during the active period in spring, becomes mixed with yellow during the summer, but during the autumn and winter rest is entirely yellow. Yellow marrow may, therefore, be regarded as red marrow in a state of quiescence. In chronic wasting diseases such as pulmonary emphysema, tuberculosis, chronic renal nephritis, and also on account of starvation nearly all the fat may be absorbed, causing the yellow marrow to have a jelly-like appearance. The fatty marrow may, on the other hand, increase accompanying eccentric atrophy of the bone until the bone becomes a mere shell and it may even float in water. This occurs especially in cases of senile osteomalacia.

The myeloplaxes or giant cells of the marrow.—The multinucleated myeloplaxes are found in Howship's crypts bordering on the marrow. They show marked powers of movement on the warm stage and also englobe particles. If carmine be injected into the marrow cavity, it is found included in the giant cells near the site of the injection. If an excess of the carmine be injected, the giant cells containing these particles are easily seen in the blood, and carmine is also found in the lungs, liver, spleen, and kidneys, showing that there is an easy exit from bone (Arnold).[22] Multinuclear giant cells are carried into the blood and appear there under a number of circumstances. But their presence in the blood does not indicate any excessive production of them in the marrow.

Lymphoid marrow.—The yellow marrow may be replaced by marrow varying in colour from a pinkish grey up to a deep red. But the lymphoid marrow as met with in disease is by no means the same as the red marrow of the young healthy animal. There is in lymphoid marrow not only a marked increase of the small colourless marrow cells and of the nucleated red cells, but many of the latter are found free in the capillaries, and there is an increase of blood pigment without there being evidence that this pigment can be worked up again as hæmoglobin. The excess of pigment is the result of hæmorrhages due to thrombosis of the bloodvessels, and this thrombosis is a sign that a destruction of leucocytes is in progress. Lymphoid marrow is best marked in pernicious anæmia, in which disease the prevailing factor is the excessive destruction of blood in the spleen and liver. In a like manner chronic septic absorption, especially chronic suppuration of bone, tends to produce lymphoid marrow. In cancerous cachexia a similar condition of the marrow may be also found, but it is necessary to distinguish lymphoid marrow from a diffuse infiltration of the marrow by secondary cancerous growths, which is often difficult. It is difficult to draw a sharp distinction between the lymphoid marrow produced by lymphadenoma accompanied by leucocythæmia and anæmia and new growths of lymphadenoid structure originating in the marrow from the small marrow cells (myeloma or lympho-sarcoma), except that these growths are circumscribed, at any rate in the earlier stages.

---

[21] Marquis: Inaugural Dissertation, Dorpat; also Centralblatt für Pathologie, &c., 1893, Band iv., S. 459.

[22] Arnold: Virchow's Archiv, 1895. Band cxl., S. 411.

The inflammatory diseases of the marrow, as compared with those of the spleen and lymphatic glands, are limited in variety, for the organisms of most infectious diseases are not arrested in the bone. Only a few kinds are so stopped—e.g., tubercle bacilli, the organisms of syphilis, and pyogenic cocci. They infect especially the ends of the long bones of young subjects in which red marrow is still present, and which are especially vascular in the neighbourhood of the epiphyses. These organisms arriving by the circulation settle down and grow, being especially favoured if a blood-clot due to some slight injury be present. In older patients the periosteum, as the most vascular part of bone in the adult, is more likely to be affected than the marrow.

LECTURE II.

Delivered on March 3rd.

THE THYMUS.

GENTLEMEN,—The thymus is a remarkable organ, since it appears under three different forms. The primary thymus is composed of glandular epithelial cells, the secondary of lymphadenoid tissue, and the tertiary of fat. The primary thymus of glandular epithelium persists in some fish and secretes mucus; in the higher animals all that normally remains of it at birth are the concentric cell masses of Hassall. But Chiari[1] has shown that the cysts of the thymus which are found in infants, and to which the names of tubercle, syphilis, and abscesses have often been given according as their contents are caseous, solid, or puriform, are really true degeneration cysts lined by epithelium. These cysts represent the mucus secreting follicles of fish, which usually shrivel up into the concentric bodies, but may be found in the kitten as cysts lined by ciliated epithelium (Capobianco, *vide infra*). Epithelial remnants may also be the source of dermoid cysts, of malignant tumours—in Rolleston's[2] case as mucus secreting cells, or as epithelioma with true nest cells in the case described by Paviot and Gerest.[3] It is this primary thymus which is so closely related in its manner of origin to the thyroid gland. The secondary thymus, composed of lymphadenoid tissue, is a paired organ in birds. In mammals it is generally fused into one mass, which may have processes running up to the trachea representing the position of the primary diverticula. It has a peculiar arrangement of lobes and lobules, which distinguishes it from compound lymphatic glands. Each lobule is divided into a polyhedral cortex, having a germinating mass of cells and a medulla in which are found the concentric bodies. It is an organ which is richly supplied with blood, and the lymphatics leading off from the sinuses round the polyhedral follicles, after passing through the glands of the superior mediastinum, join the thoracic and right lymphatic duct to enter the veins of the neck. This lymphadenoid thymus, which commences to develop and remove the primary one about the fourth month, reaches its fullest development at birth. It certainly forms leucocytes, and during embryonic life at least red cells also, even in the highest mammals. The formation of leucocytes takes place earlier in the thymus than in the lymphatic glands. The thymus was first removed by Friedleben,[4] and his experiments have lately been repeated by Tarulli.[5] The young animals did not suffer from the loss. After birth it persists for a variable length of time up till puberty before it changes into the tertiary fat organs. It persists throughout life as a lymphadenoid organ in some fish and reptiles, and may be met with in man long after puberty. The thymus may be diseased at birth owing to the cysts already mentioned. If hæmorrhage into these cysts or inflammation sets in rapidly increasing dyspnœa may ensue (Durante[6]), and the organ being hidden behind the sternum the cause of the dyspnœa may remain unsuspected. Sudden death from asphyxia frequently occurs from this cause in newborn infants and young children, and the enlarged thymus is only discovered post mortem. A large lymphadenoid thymus may be met with in adults associated with enlarged thyroid, and may form an additional unsuspected cause of dyspnœa which is not relieved by an operation upon the thyroid. Perhaps the pressure on the large veins at the root of the neck causes venous congestion and enlargement of the thymus, as happens in the spleen from similar causes The thymus is also enlarged in the cases of lymphadenoma to be afterwards referred to. The tertiary fat thymus is always to be found in man, the peculiar lobulation of the fat showing that it has been derived by a metamorphosis of the lymphadenoid organ (Waldeyer,[7] Capobianco[8]). The fat is, however, but a quiescent stage of lymphadenoid tissue as is the yellow marrow of bone, and so reappearance of the lymphadenoid tissue takes place in adults suffering from lymphadenoma. A large lymphadenoid thymus is met with in diseases accompanied by anæmia, such as Addison's disease and the acromegaly of Marie, &c. Epithelial cell groups and small cysts were noted by Acland[9] having the position of Horsalle's bodies in two young persons, both of whom had been anæmic, one had suffered from hæmophilia, the other from purpura. There is some antagonism between the thyroid and thymus gland. The thymus is well developed in cretins; feeding with the thymus gland relieves exophthalmic goitre.[10]

---

[1] Chiari: Zeitschrift für Heilkunde, 1894, Band xv., s. 403.

[2] Rolleston: Journal of Pathology and Bacteriology, 1896, vol. iv., p. 228.

[3] Paviot et Gerest: Archives de Médecine Expérimentale et d'Anatomie Pathologique, 1896, tome viii., p. 606.

Siegel cured a child aged two and a half years threatened with asphyxia by displacing the enlarged thymus from the anterior mediastinum into the subcutaneous tissue.[11]

---

[4] Friedleben: Die Physiologie des Thymusdrüse in Gesundheit und Krankheit. Frankfort, 1858.

[5] Tarulli: Atti dell' XI. Congresso Medico Internazionale, Roma, 1894, vol. ii., Fisiologie, p. 19.

[6] Durante: Comptes rendus de la Société de Biologie, 1896, p. 282.

[7] Waldeyer: Sitzungsberichte der Akademie der Wissenschaften, Berlin, Band xxv., s. 433.

[8] Capobianco: Archives Italiennes de Biologie, 1892, vol. xvii., p. 55.

[9] Acland: Pathological Society's Transactions, 1885, vol. xxxvi., p. 491.

[10] Owen: Brit. Med. Jour., vol. ii., 1896, p. 1017.

[11] Centralblatt für Chirurgie, 1896, S. 1141.

LYMPHATIC GLANDS.

True lymphatic glands are only found in birds and mammals. The thymus supplies their place in the lower forms. There are also lymphadenoid masses in connexion with the kidney of fish ; the salamander has lymphadenoid tissue round its liver. In the frog the thymus early changes into fat, and the spleen has no Malpighian bodies, but there are besides the marrow, which is red in the spring, also rudimentary tonsils and the fat bodies in the abdomen, which are during part of the year lymphoid in structure. Lymphatic glands are few and small in rodents, more numerous in the carnivora and ungulates, but most numerous in man (Gulland[12]). In some mammals, such as the sheep, small glands, intermediate between the spleen and lymph glands, are found in front of the vertebræ in the mesentery and contain blood in them, the so-called hæmolymph gland.[13] But they have not been shown to exist in man. Lymphatic glands are developed relatively late in embryonic life, they do not appear until after the middle of this period—i.e., after the thymus has become developed as a lymphadenoid organ. Lymphatic glands vary much, some having only a single follicle forming a minute mass from 1 to 2 mm. in diameter. There are others with more than one follicle varying in number up to the ordinary compound lymphatic gland. Lymphatic glands undergo retrograde metamorphosis, especially in old age, and turn into fat like the bone marrow and thymus. But at any time they may be excited to regeneration, a compound gland may develop from a single follicle, or a new formation of lymphatic glands take place in connective tissue. The process is the same as in the embryonic formation, leucocytes emigrate into the connective tissue and split up its fibres into retiform tissue. The only difference in the lymphadenoid tissue arising from the excitation of diseased products is that the arrangement of germ centres is not so well defined as in the normal gland.

Lymphatic glands have two functions, the production of leucocytes and the protection of the circulation from the entrance of organisms through the skin and mucous membranes. Organisms may be carried to a gland where they are arrested and ultimately destroyed, or they may grow through the gland, destroying it meanwhile, and so reach the circulation. But those of the highest virulence either enter by the bloodvessels and so escape the lymph glands or they pass at once through the gland without stopping and without setting up any reaction. Besides the lymphatic glands, through which all lymph has to pass, the mucous membranes of the respiratory and alimentary canal have a further means of preventing the entrance of organisms and their products in the shape of follicles situated in it, and there is also a considerable development of the tissue in the mucous and sub-mucous coats not specially gathered up into follicles, but diffused throughout it. This development of lymphadenoid tissue becomes more striking when we see how slight is the development of lymphadenoid tissue in connexion with the pelvis of the kidney, the ureters, and the bladder, and the absence of lymphadenoid tissue in connexion with the cerebro-spinal lymph spaces. The cerebro-spinal fluid is practically lymph in an extensive system of sinuses, yet this lymph passes directly into the venous blood, and there are therefore cell products or metabolites due to brain activity which do not need to be rendered harmless before they are allowed to enter the circulation. A diffuse form of lymphadenoid tissue is met with in the mucosa and sub-mucosa of the conjunctivæ, nose, pharynx, larynx, bronchi, stomach, and intestines, in some parts less marked than in others—e.g., in the œsophagus; but in all parts capable of being abnormally developed in the course of disease. Of the special masses of lymphadenoid tissue the palatal tonsils develop around epithelial sacs which remain as the crypts. The pharyngeal tonsil forms around the epithelial crypt developed in connexion with the hypophysis, and the lingual tonsil is a lymphadenoid mass about the foramen cæcum. The solitary and agminated follicles develop in the mucosa between the glandular epithelium of the ileum, cæcum, and appendix. But the function of this tissue is not limited to arresting or rendering harmless materials about to be absorbed, the follicles also produce cells which freely pass into the mouth, intestine, and bronchi, and prevent the excessive development of organisms in these canals. Foreign bodies can easily enter through an intact mucous membrane, whereas in the case of the skin there must be a lesion of the surface or the material must be well rubbed into the mouths of the hair follicles and sweat glands. Coal dust when inhaled passes through the intact epithelium of the bronchi and alveoli to the neighbouring glands. Carmine which has been mixed with the food of the animal passes out through the intact wall of the intestines, especially by way of the solitary and agminated follicles. Of all micro-organisms the tubercle bacillus has yielded most interesting experimental results. If a culture of tubercle bacilli be injected into the trachea of an animal the bacilli pass through the intact mucous membrane and infect the neighbouring glands. Similar results may be obtained by feeding animals on material containing tubercle or anthrax bacilli, which pass through the uninjured intestine. In the human subject in connexion with tuberculous glands in the neck a visible lesion in the mouth or on the tonsil is quite the exception, a carious tooth being the only frequent one. Indeed, the local inflammation causing hypertrophy of the tonsil or adenoid vegetations seems very rarely to be followed by tuberculous glands in the neck. It is quite the exception to see a combination of hypertrophied tonsils or adenoid vegetation and tuberculous glands in the same patient.

---

[12] Gulland: Development of Adenoid Tissue, especially the Tonsil and Thymus; also Nature and Variety of Leucocytes, Laboratory Reports of the Royal College of Physicians of Edinburgh, 1891, vol. iii.; also The Development of Lymphatic Glands, Journal of Pathology and Bacterlology, 1894, vol. ii., p. 447.

[13] Vincent and Harrison: Journal of Anatomy and Physiology, 1897, vol. xxxi., p. 176

Lymphatic glands and follicles may be affected through the circulation, like the spleen and bone marrow. The affections are generally sub-acute or chronic rather than acute. The specific fevers, syphilis, and tubercle when generalised, may cause a widespread enlargement. The acutest form of general enlargement is the hæmorrhagic swelling characteristic of plague. More frequently diseases are due to direct infection of the follicles and infection of the glands by way of the lymphatics. In acute inflammation there is an increased circulation through the gland with a more rapid production of cells. The inflammation may subside owing either to the destruction of the organisms or because the infection has passed on through the gland into the circulation. One of or all the follicles of the gland may pass from the stage of inflammation to that of suppuration, which may extend outside the gland, the lymphadenoid tissue forming a slough in the centre. This is often seen in gonorrhœal buboes and in the intestinal follicles. Another form of acute inflammation is due to streptococci, as in diphtheria, scarlet fever, and erysipelatous complications; there is then marked infiltration of the gland and the surrounding connective tissue with œdema and fibrin. A chronic inflammation of lymph glands and follicles consists at first of a simple overgrowth of the gland formed chiefly by an increased number of cells in the meshes, and the distinction between the germ follicles and the medulla is less clearly marked. But if the chronic inflammation continues there is an increase in the connective tissue derived from the capsule and septa of the gland, and thus the amount of lymphadenoid tissue, including cells, becomes really diminished although the gland may be apparently enlarged. The stopping power of lymphatic gland tissue varies with the different diseases. Thus, in syphilis, although the gland enlarges there is no evidence of any power of arresting disease. The attempt to arrest syphilis by excising the hard sore and the glands has been a complete failure. On the other hand, it seems to have a considerable power in preventing the extension of tubercle. Usually the tubercle bacilli are caught in the germ follicle, where they form tubercles which afterwards caseate. Less often there is no definite formation of tubercle, or indeed of giant cells, nor is there any early tendency to caseate, but diffuse infiltration of the whole gland structure. It is then extremely difficult to distinguish a gland so affected by tubercle from lymphadenomatous glands by simple microscopic examination, although inoculation if successful may demonstrate the disease to be of a tuberculous nature. Repair and healing take place in lymph glands by scar tissue derived from the connective tissue, capsules, and septa, the lymphadenoid tissue proper taking no share in it.

LYMPHADENOMA.

Lymphadenoma is a suitable term for those affections the various forms of which have one feature in common—viz., a growth of lymphadenoid tissue closely resembling in structure that of lymphatic gland. The subdivisions of lymphadenoma are excessively confusing from the tendency to classify by some one prominent feature and from the desire of splitting up clinical cases into an endless number of groups. The names in use are employed in very different senses, and it would be difficult to find any two cases of a series which do not exhibit striking differences. We must anticipate in the classification of cases of lymphadenoma the recognition of its definite cause, and as there are many indications that the causes are not very far separated from that of syphilis and tubercle we can take as our guide the analogy of tubercle and distinguish a local disease, local lymphadenoma, from a general disease. generalised lymphadenoma or lymphadenomatosis, in which lymphadenoid tissue is involved in widely separated positions, although to a very varied extent. Of local lymphadenoma we may further mark out two kinds, one simple or benign local lymphadenoma, in which the cause is apparently more or less continuously acting upon the lymphadenomatous tissue from the surface of the mucous membrane or skin; whereas in the more malignant form, malignant local lymphadenoma, there is a lack of evidence as to the external source of the irritation, or such irritation as may be present is inadequate, the essential feature being the continuous proliferation of cells from some cause which must be within the tumour itself. So also in generalised lymphadenoma or lymphadenomatosis we can recognise the local origin of the growth from some cause which widely affects lymphadenoid tissue, but in which the development of the disease can be controlled by treatment, and, on the other hand, a malignant generalised lymphadenoma in which the cause must reside within the growths themselves as in other forms of cancer. In a tabular form, then, the divisions of lymphadenoma are: (*a*) Local lymphadenoma: (1) simple or benign; and (2) malignant. (*b*) Generalised lymphadenoma or lymphadenomatosis: (1) benign; and (2) malignant. The other names in common use—leucocythæmia or leukæmia, pseudo-leukæmia, Hodgkin's disease, and lymphosarcoma—I can affirm from an examination of the literature of the subject to be used scarcely by any two writers in the same sense. The term "Hodgkin's disease" should be employed as synonymous with "lymphadenoma"; Dr. Hodgkin's paper is entitled "Some Morbid Appearances of the Absorbent Glands and the Spleen." He did not describe any such a well-defined disease as, for instance, did Dr. Addison. The attempt to apply his name to any special form of lymphadenoma cannot be sustained. Leucocythæmia or leukæmia (some writers distinguish the two) are names for one of the signs of the disease which may be present or absent, or absent in the early stages, present later, and finally disappear before death. It has often been used as a name without there being evidence that the blood was even examined; its existence may have been overlooked where only one examination has been made, on account of the sudden variations. An increase of leucocytes may arise from some temporary inflammatory cause or be merely relative owing to the diminution of red cells. Some writers call a slight increase of white cells leucocytosis, some call it pseudo-leukæmia, and others use the term pseudoleukæmia when no increase of white cells was noticed. Another complexity has been added since the division of the white corpuscles, for which we are indebted to Professor Ehrlich. From a careful comparison between the microscopical examination of the blood. the clinical features of the disease, and the results of the necropsy I do not believe that we can decide from the examination of the blood alone as to the parts of the lymphadenoid organs specially affected. For instance, cases have been called "myelogenous leucocythæmia" from one examination of the blood in the entire absence of clinical and post-mortem confirmation. Lymphosarcoma is a term liable to be confounded with sarcoma growing in a lymphatic gland. It is often used as indistinguishable from lymphadenoma; for instance, we read of multiple "lymphosarcoma" being cured by arsenic. Dr. Wilks[14] was really the first to bring this subject of lymphadenoma forward. and it was after his earlier observations had been made that he lighted on Hodgkin's paper, which had until then received no attention. His name "anæmia lymphatica" for the generalised form is better than "leucocythæmia," seeing that it is the decrease of red cells and not the increase of the white ones which is the more important. The only rational way at present of grouping the various cases of lymphadenoma is by taking the point of origin in each case. Although we remain as yet ignorant as to the causes, yet by considering the probable ways of entry we shall be prepared to receive further evidence of causation without having to make extensive changes in the system of classification. This will be much better than naming the case after some one particular sign of the disease which happens to be prominent.

---

[14] Wilks: Guy's Hospital Reports, 1856, p. 103; 1859, p. 109; and 1865, p. 56.

LECTURE III.

Delivered on March 5th.

Illustrations of the Local Commencement of Lymphadenoma.

Conjunctiva.—Trachoma forms a common illustration of an infection producing lymphadenomatous nodules. Lymphadenoma may occur in the eyelids. A boy had growths of the orbit and of the parotid region with leucocythæmia (Fröhlich).[1]

Nose.—In the nose overgrowth of the mucous membrane covering the inferior turbinals is very common, the result of local irritation. Occasionally it forms the starting place of a lymphadenomatous growth—e.g., in a case described by Rosenberg,[2] which became generalised, and death occurred in two and a half years from the commencement.

Tonsil.—On account of local irritation this organ is constantly seen in a condition of overgrowth. It may assume a malignant form, projecting as a tumour, capable at first of being shelled out, or extension may take place to the deep glands of the neck[3] or by rapid infiltration into the surrounding tissues of the fauces and pharynx.[4] Lymphadenoma may start in the tonsil, and after involving the glands in the neck become generalised.[5]

Pharynx.—Adenoid vegetations, a local overgrowth, is the common result of irritation. Occasionally a case commencing in this way spreads so as to involve the pharynx and larynx, and then the disease becomes generalised (Chiari).[6] General hypertrophy of the fauces and pharynx is not uncommon, consisting of a simple overgrowth; cases, however, like those of Störk[7] are of a more malignant type, rapidly infiltrating the whole wall, causing anæmia, hæmorrhages, &c.

Larynx.—Measles and other infectious diseases may leave behind a hypertrophic laryngitis due to overgrowth of lymphadenoid tissue. In a case described by Stieda[8] there was found post mortem a general swelling of the ventricular bands and epiglottis with lymphadenoid tissue, also a general enlargement of the lymphatic glands and follicles.

---

[1] Fröhlich: Wiener Medicinische Wochenshrift, 1893, Band xliii., S. 285. et seq.

[2] Rosenberg: Verhandlungen der Berliner Medicinischen Gesellschaft, 1895, Band xxv., pt. ii., S. 341.

[3] Barker: Transactions of the Pathological Society, 1886, vol. xxxvii., p. 218.

[4] West: Ibid., 1882, vol. xxxiii., p. 331.

[5] Nash: Brit. Med. Jour., vol. ii., 1892, p. 1054.

[6] Chiari: Internationales Centralblatt für Laryngologie, 1895, S. 381.

[7] Störk: Wiener Medicinische Wochenschrift, 1894, Band xliv., S. 1697 et seq.

Stomach and intestine.—It is well known that certain infectious diseases markedly affect the lymphadenoid tissue of the alimentary canal, especially the solitary and agminated follicles such as typhoid fever, anthrax, and the enteritis of swine. Less well known are the inflammatory changes in the intestinal follicles and the mesenteric lymph glands in diphtheria. In children after death from typical laryngeal diphtheria requiring tracheotomy Colman[9] found marked hyperæmia and enlargement of all the solitary follicles and Peyer's patches and mesenteric glands, no diphtheritic membrane or bacilli or ulcerations being present. The cases of lymphadenomatous disease of the stomach and intestine have been collected by Newton Pitt[10] as follows: (1) A local tumour; (2) congestion and ulceration from hæmorrhage with leucocythæmia; (3) a new growth arising in the mucous and sub-mucous tissue and projecting into the lumen, especially from the lymphadenoid follicles in the cæcum and appendix; and (4) a widespread overgrowth infiltrating the coats of the bowel and forming a kind of sheath, leading to constriction or paralytic dilatation. No doubt in a number of cases it is difficult to know when the disease commenced, and, on the other hand, owing to early obstruction or perforation or other complication, the disease may never have time to become widely generalised. (Moore,[11] Hadden).[12] Yet all kinds of extension to the glands spleen, &c., are met with. A frequent origin of the condition is the chronic intestinal catarrh of children, in which, however, tubercle and lymphadenoma are difficult to distinguish. In some cases there has been distinct evidences as to causation. In Taylor's[13] case lymphadenoma of the small intestine followed upon typhoid fever. Coupland's[14] case of malignant lymphadenoma of the stomach was preceded by dyspepsia and inflammation of the bowels. The disease extended to the retro-peritoneal glands, then to the kidneys, ovaries, thyroid, and intra-muscular tissue of the thigh.

Bronchial and posterior mediastinal glands.—In no place where it occurs is the local origin of lymphadenoma more clearly marked. The very fact that it is so frequently found along with some signs of tuberculosis in the lung shows that although not of tuberculous origin it is much of the same kind. Another sign of preliminary excitation is the black pigment contained in the growth. The over-growth not only includes the actual lymphatic glands, but also the lymphadenoid tissue around the bronchi. The growths may rapidly compress the air-tubes and prove fatal before such extension. Yet when it happens to compress the lungs rather than the bronchi much greater extension may occur. Thus in Chaplin's[15] case after influenza—and this has been a common cause—dyspnœa and anæmia followed, and there was found post mortem a mass of glands around the bronchi extending into and infiltrating the right lung, whilst in the left lung were some caseating tuberculous nodules. The cervical, axillary, inguinal, and lumbar glands were enlarged, but not caseating. The spleen was characteristically lymphadenomatous. If we take three of Turner and Sutton's cases[16] we have instances of different types, but all three affording indications as to their primary origin. In a boy aged ten years there were cheesy masses in the apices of the lungs, enlarged mediastinal axillary, submaxillary, and inguinal glands, some hard, others soft, and the kidneys were enlarged and infiltrated, but not the liver and spleen. The boy had suffered from purpuric eruption, ecchymosis, and anæmia, clear evidence that there had been also leucocythæmia. A man aged thirty-six years, who had suffered from syphilis and had been addicted to drink, had caseous and fibroid changes in the lungs, a mass of glands compressing the right bronchus. He had had leucocythæmia and showed thrombosis of the iliac veins, embolism of the middle cerebral artery, and the spleen was enlarged with firm masses in it. A woman aged twenty-four years commenced by suffering from pleurisy and pericarditis, which were followed by faintness after food, morning retching, stabbing pain in the chest, and dysentery. The pleura and pericardium were thickened and, together with the right lung, infiltrated by greyish nodules, the bronchial, cervical, and lumbar glands were enlarged and softened, and the spleen, liver, and kidneys infiltrated by semi-gelatinous nodules.

---

[8] Stieda: Archiv für Laryngologie, 1896, Band iv., S. 46.
[9] Colman: Transactions of the Pathological Society, 1888, vol. xxxix., p. 122.
[10] Newton Pitt: Ibid., 1889, vol. xl., p. 80.
[11] Norman Moore: Ibid., 1883, vol. xxxiv., p. 99.
[12] Hadden: Ibid., 1886, vol. xxxvii., p. 234.
[13] Taylor: Ibid., 1877, vol. xxviii., p. 135.
[14] Coupland: Ibid., 1877, vol. xxviii., p. 126.

The thymus.—The thymus is also the subject of lymphadenomatous enlargement, and this is clearly distinguishable from the condition of cystic and hæmorrhagic enlargement at birth by the fact that other lymphadenoid tissues are involved. Thus in a woman aged twenty-nine years there was great enlargement of the thymus along with a similar condition of the supraclavicular and axillary lymphatic glands (Brigidi and Piccoli).[17] In a child, aged nine years, besides the thymus, which formed the greatest enlargement, there was also enlargement of the spleen and the intestinal follicles, together with nodules in the liver (Eberth).[18] In the case of a woman who died shortly after removal of a goitre the thymus was found enlarged as well as the tonsils, both palatal and lingual, and the intestinal follicles (Schnitzler).[19] Virchow[20] said that he had seen a number of cases occurring in young recruits which began in the thymus. Of course, it is possible for a malignant tumour to begin in the thymus and yet not be lymphadenoid in character, as in the case described by Rolleston of a hæmorrhagic adeno-chondro-sarcoma, the glandular portion having the appearance of being derived from mucous glands like the parotid; the tumour in this case clearly grew from remains of the primary thymus to which Hassall's corpuscles belong. The growths in the thymus and anterior mediastinum are usually fatal at an early period before much generalisation has occurred owing to tracheal and bronchial pressure.

---

[15] Chaplin: Ibid., 1893, vol. xliv., p. 13.

[16] Turner and Sutton: Ibid., 1878, vol. xxix., p. 343.

[17] Brigidi and Piccoli: Beiträge zur Pathologischen Anatomie und zur Allgemeinen Pathologie, 1894, Band xvi., S. 388.

The axilla.—Chronic enlargement of the lymph glands from irritation entering the lymphatics from the hand and also from the breast may be found tuberculous on exploration. In other cases it may be recognised as the starting-point of lymphadenoma. I have had two cases under my care lately in both of which the enlarged glands were certainly neither tuberculous nor malignant. They showed on section lymphadenoid and fibrous tissue, and portions had so intimately ensheathed the bloodvessels as to be irremoveable.

Neck.—Lymphadenoma frequently commences in the neck. In some cases it is possible to assign a cause, such as a carious tooth, a purulent discharge from the ear, or repeated inflammations of the tonsils. It may start as an acute or sub-acute glandular inflammation, something like mumps,[21] which suggests a specific cause reaching the glands by the lymphatics. It is most difficult to distinguish from tubercle except by the tendency to caseation on the part of the latter. As I have before mentioned, this caseation is absent in the diffuse form. I have had lately a man under my care with enlargement of the glands on both sides of the neck of an indolent character. As arsenic was of no avail I removed some. There was no evidence of caseation, but from the microscopical structure the appearance was either that of diffuse tubercle or an endothelial new growth, but the latter was excluded by the time the disease had lasted. A case of lymphadenomatous glands in the neck which I have long had under view is interesting as standing intermediate between a local and generalised lymphadenoid. A middle-aged man was under my colleague Dr. de Havilland Hall with a lymphadenomatous mass in the neck. For some time arsenical treatment kept the growth in check, but later the enlargement continued in spite of the treatment, and I removed all that I could of the growth, leaving some masses about the large vessels in the root of the neck. After the operation he was again put on arsenic, and although the lymphadenoma has never quite gone it has for some years not advanced. Unfortunately, the man cannot continue a course of arsenic very long without sickening of the drug and then he has to rest awhile. The most malignant form of lymphadenoma may commence in the neck. A girl (under Durham[22]) first felt the neck stiff and tender after sleeping in a damp bed. The enlargement commenced below the jaw, soon ulcerated, and then formed a large oval ulcer, infiltrating the muscles of the neck. After death an enlarged mass was found surrounding the upper part of the abdominal aorta behind the stomach and pancreas, involving the mesenteric and lumbar glands.

---

[18] Eberth: Virchow's Archiv, 1870, Band xlix., S. 63.

[19] Schnitzler: Status Thymicus, Wiener Klinische Wochenschrift, 1894, No. 20.

[20] Virchow: Berliner Klinische Wochenschrift, 1891, S. 1185.

[21] Dawson Williams: The Lancet, Jan. 16th, 1897, p. 160, and others in following numbers on A Glandular Fever of Childhood.

The groin.—The groin is not uncommonly the starting place of lymphadenoma of various forms Sometimes evidence of a source of irritation is found, such as venereal disease, strain, or septic absorption from the leg. A chronic indolent enlargement is seen in hot climates, of obscure origin, often called malarial. As compared with the gland in the neck the rarity of tubercle is remarkable, and on this account the diagnosis of lymphadenoma is made easier. I saw, however, not long ago a young man who had been put under an anæsthetic in order to remove a mass of glands supposed to be tuberculous. The operation was not begun owing to enlargement of iliac and lumbar glands being discovered. I suggested the administration of large doses of arsenic, and the glands both in the groin and in the lumbar region quickly subsided. Unfortunately, however, lymphadenoma of the groin has a great tendency to become generalised and to show malignant characters. In Taylor's[23] case the lymphadenoma commenced as a lump in the groin, and this was followed by swelling of the leg, general enlargement of the lymphatic glands, especially those of the parotid and sub-maxillary regions, and was attended by fever but not by leucocythæmia. The liver was found at the post-mortem examination to be enlarged, but not the spleen. On the other hand in Greenfield's[24] case, the spleen, lungs, and skin were affected from a growth in the groin, but not the other lymphatic glands. The lymphadenoma may remain local, but infiltrate most widely around after a malignant fashion. In Lediard's[25] case there had been a lump in the groin for three years, then it ulcerated and formed a bleeding mass, which caused extreme anæmia accompanied by fever and vomiting. No other growths were discovered post mortem. In Morton's[26] case the enlargement began symmetrically and simulated at first chronic recurrent inflammation. Later, the growth extended and infiltrated the muscles of the abdominal wall and surrounded the large vessels. The lungs were found studded with secondary growths. There are, however, many cases of lymphadenoma in the groin which are not malignant in the earlier stages, and which either yield to drugs or admit of removal. Even when the lumbar glands have been enlarged behind the peritoneum they have been successfully shelled out (Marconi).[27]

---

[22] Durham: Transactions of the Pathological Society, 1883, vol. xxxiv., p. 245.

[23] Taylor: Clinical Journal, 1896, vol. viii., p. 33.

[24] Greenfield: Transactions of the Pathological Society, 1876, vol. xxvii., p. 275.

[25] Lediard: Ibid., 1886, vol. xxxvii., p. 472.

The spleen and bone marrow, especially the former, are involved when lymph-adenoma becomes generalised, and hence there are endless varieties of combinations with enlarged lymph glands and with leucocythæmia.

Spleen.—The commencement of lymphadenoma in the spleen is very questionable. The cases in which the spleen is the chief organ involved are mostly diseases which have in all probability entered through the alimentary canal, or are due to some other general infection through the circulation. Enlargement of the spleen is common in young children and sometimes seems due to nothing more than bad feeding. Upon suitable nourishment and arrest of intestinal catarrh the spleen subsides. However, if the case is not taken early generalised lymphadenoma soon sets in with anæmia, leucocythæmia, and enlargement of lymphatic glands and follicles. Malaria and malarial affections are another common source of lymphadenoma; the spleen remains enlarged after the malaria has subsided. Wilson[28] has recorded cases occurring in three generations of the same family in which there were enlargement of the spleen and anæmia, but without leucocytosis or enlarged lymph glands. There is considerable practical importance in the distinction because a spleen enlarged simply as the result of malaria has been frequently removed with success; on the other hand, all cases of splenectomy in generalised lymphadenoma with leucocythæmia have failed. The changes produced in lymphadenoma in the spleen are of two kinds. In one form the Malpighian bodies stand prominently out as white or yellowish masses, which are hard to distinguish from tubercle. In other cases the enlargement is of the diffused variety, soft when the overgrowth is mainly of lymphadenoid tissue, hard when mainly of connective tissue from the capsule and septa This latter form also contains much pigment and is difficult to distinguish from a spleen the result of malaria. In cases of lymphadenoma accompanied by leucocythæmia the spleen, besides being much enlarged, is liable to wedge-shaped infarcts. The local enlargement of the spleen occurring by itself, having no obvious connexion with any affection of the other lymphadenoid tissue or with the blood, has been called primary splenomegaly. The growth is slow, and cases have been submitted to splenectomy successfully. It is not very clear, but apparently it is the cells of the splenic pulp which multiply and compose them. The interest lies, then, in the slow and local growth of the primary tumours. In this respect it may be compared to some of the tumours of bone.[29] The carcinomas and sarcomas of the spleen are secondary growths.

---

[26] Morton: Ibid., 1895, vol. xlvi., p. 162.

[27] Marconi: Successful Removal of a Lympho-sarcoma with Resection of 3 c.m. of the Inferior Vena Cava, Centralblatt für Chirurgie, 1894, p. 334.

[28] Wilson: Transactions of the Clinical Society, 1893, p. 163.

Bone marrow.—It is in generalised lymphadenoma that the bones are affected, but there is this marked distinction, that beyond the change to lymphoid marrow the bones show only tenderness, temporary swelling of the soft parts, and pain. There is no enlargement like the spleen. In such cases the spleen is generally enlarged, also very often all lymphadenoid structures, and there is leucocythæmia. I doubt very much the existence of the so-called "pure myelogenic leucocythæmia." Returning now to the new formations allied to lymphadenoma, a simple circumscribed tumour may commence and grow slowly, without at first causing any marked enlargement of the bone, but rather replacing the bone framework and the marrow cavity by a very delicate, moss-like bone. Owing to the absence of a distinct enlargement notice may first be drawn to the growth by the occurrence of a spontaneous fracture owing to the replacement of the bone by the tumour. In structure the growth consists of small, round cells with a variable amount of newly formed connective tissue into which hæmorrhages may occur. In other cases the tumours are multiple in one or many of the bones of the skeleton, appearing as discrete tumours through which the knife easily cuts, or there are secondary changes resulting in hæmorrhages or cyst formation. or pathological fractures (Herrick and Hektoen,[30] Kahler[31]). Generalisation takes place in some cases very early and in others only late. These generalised forms connected especially with bone marrow assume three types—one approaching cancerous osteomalacia, one approaching osteitis deformans, and one in which leucocythæmia is the prominent feature. But in all there is some enlargement of lymphadenoid tissue in the lymphatic glands, spleen, &c. Nothnagel's case[32] was of an osteomalacic type. Pain began in the sternum and was attended by wasting, sweating, and irregular fever. The pain spread to the bones of the trunk and extremities, besides which there was anæmia, swelling of the spleen, and enlargement of the lymphatic glands, but there was no leucocythæmia. The bones especially affected were the scapula, clavicle, ribs, vertebræ, sternum, pelvis, and the metatarsal and metacarpal bones. On post-mortem examination the fatty marrow was found to have been replaced by greyish-white material interspersed with long septa The tissue consisted of small round cells and contained blood pigment. On maceration the bones appeared of a spongy material like moss which had filled the marrow cavity. Moore, Hammer. and Goodhart's cases are closely related or show intermediary stages with osteitis deformans. In Moore's[33] case the skull was infiltrated by small round cells and the cervical lymph glands were enlarged. In Hammer's[34] case the skull and vertebræ were much thickened and the spleen and lymphatic glands were enlarged. Goodhart[35] described a typical case of osteitis deformans with nodules of lymphadenoid material in the spleen, liver, pleura, and in the mediastinal and abdominal glands. Leucocythæmia was a prominent symptom in the following cases. A woman suffered from symptoms of anæmia, erythema nodosum, and rapid cachexia. At first she had amenorrhœa and then profuse uterine hæmorrhages. There was great tenderness of the sternum, the ribs were slightly tender, and the red corpuscles were to the white as 5 to 1. At the post-mortem examination there were many small hæmorrhages, but no enlarged lymphatic glands. The spleen weighed 10 oz The skull cap was very heavy and dense and the cavity of the femur was full of red lymphoid marrow (Beatty).[36] Grawitz[37] described a similar case which he called malignant osteomyelitis attended by marked anæmia and metastasis. In Zahn's[38] case there were lymphatic tumours with softening of the bones, curvature of the vertebræ, and spontaneous fractures of the ribs. In Weber's[39] case, a man aged forty years, who had had syphilis, died exhausted after one and a half years' illness. The sternum was enlarged and bent with the ribs so as to compress the aorta, and these bones with the vertebræ contained reddish tissue. The cranium had many rounded spots the size of a threepenny-piece. There was amyloid degeneration in the kidneys and spleen. The new tissue consisted of small round cells. Comparable to the primary tumours of the spleen called splenomegaly, are the well known giant-celled myelomas or myeloid sarcomata, which grow from the marrow at the ends of the long bones and in the short and flat bones. But as distinguished from the small celled myelomas or lymphadenomas of the bone-marrow above noted they show no tendency to involve the other lymphadenoid tissues. A further resemblance between the spleen and marrow is to be found in the fact that carcinomas and sarcomas of the bone-marrow are likewise secondary growths.

---

[29] See many of the cases of successful splenectomy—e.g., Knowsley Thornton: Multilocular Cystic Tumours of the Spleen, Transactions of the Pathological Society, 1884, vol. xxxv., p. 385; Bruhl: De la Splénomégalie primitive, Archives Générales de Médecine, 1891, tome 167, p. 673, and tome 168, p. 160; Picou et Ramond: Splénomégalie primitive, Archives de Médecine Expérimentale et d'Anatomie Pathologique. 1896, tome 8, p. 168. The enlarged spleen removed successfully by Mariott (Museum of the Royal College of Surgeons of England, No. 2866 A) was found to be tubercular in structure.

[30] Herrick and Hektoen: Medical News, Philadelphia, 1894, vol. ii., p. 239.

[31] Kahler: Prager Medicinische Wochenschrift, 1889, Nos. 4 and 5; also Centralblatt für Chirurgie, 1889, p. 451.

---

[32] Nothnagel: Lymphadenia Ossium, Virchow's Festschrift, 1891, Band ii., S. 155.

[33] Norman Moore: Transactions of the Pathological Society, vol. xxxvi., 1885, p. 393.

[34] Hammer: Primäre Sarcomatose Osteitis mit Chronischen Rückfallsfieber, Virchow's Archiv, 1894, Band cxxxvii., S. 280.

[35] Goodhart: Transactions of the Pathological Society, vol. xxxix., 1888, p. 262.

[36] Beatty: Academy of Medicine of Ireland, March 6th, 1891.

[37] Grawitz und Zahn: vide Markwald, Virchow's Archiv, 1895, Band cxli., S. 128.

[38] Ibid.

[39] Parkes Weber: Transactions of the Pathological Society, 1896.

THE COMPLICATIONS WHICH ATTEND LYMPHADENOMA.

Fever.—Any form of lymphadenoid enlargement may be attended by fever the result of cell destruction and of the absorption of the products. The characteristic fever of tonsillitis and other glandular affections, of typhoid fever, malaria, and relapsing fever are well known. In cases of generalised lymphadenoma a fever of the continuous or intermittent type, but generally irregular, occurs, and is accompanied by profuse sweating and general exhaustion.

Leucocythæmia and anæmia.—I have already referred to the fact that an excessive production of white cells provokes destruction of red cells and also intravascular coagulation. Infarcts occur especially in the spleen, the capillaries of mucous membranes and of the cerebral arteries, &c., become choked with white corpuscles, and ulceration and hæmorrhages ensue. The patient may die from recurrent epistaxis, cerebral hæmorrhage, perforation, &c. Fatal cerebral hæmorrhage may thus occur in young patients.

Fatal results of the pressure of lymphadenomatous masses.—Growths in the mediastinum press on the trachea and bronchi. The stomach or intestines may be compressed, intestinal obstruction ensue, or absorption by the lacteals be prevented. The heart and large bloodvessels may become surrounded by a solid mass which impedes the circulation. Compression upon the arteries, veins, and lymphatics affects important organs such as the liver and kidneys. Moreover, these organs may be infiltrated diffusely with small round cells which compress the actual gland cells and cause them to degenerate, so that the function of the gland may easily be much more impaired than the external appearance of the organ might lead one to suppose.

Lymphadenoma in animals.—The various forms of lymphadenoma are met with also in animals. I had a cat which suffered from marked anæmia and leucocythæmia; its spleen weighed one-tenth of the whole animal, whereas the spleen of a normal cat weighed on the same day was only $\frac{1}{432}$ part. A dog I examined had a lymphadenomatous mass which began in the posterior mediastinal glands and compressed the trachea and bronchi. A similar mass in another dog arose from the præ-vertebral abdominal glands and surrounded the lower end of the aorta and the iliacs. Reinländer[40] has noted lymphadenoma with leucocythæmia in the horse.

Lymphadenoma in relation to tubercle.—There must be some close connexion between lymphadenoma and tubercle, for in the majority of post-mortem examinations some distinct tuberculous lesion has been found and in many it has been impossible with the naked eye to distinguish what is lymphadenomatous from the tubercle. The absence of caseation is no disproof of tubercle, nor does the absence of giant cells on microscopical examination exclude the diffuse form of tubercle. The inoculation test is also liable to several fallacies—e.g., if both tubercle and lymphadenoma be present the tubercle bacilli may easily get into the blood or lymph passing through a lymphadenomatous mass. There appears also another similarity in these mixed cases of lymphadenoma and tubercle; both affections appear to start from the same place, whether this be through the throat, neck, lungs, or intestines. One of the first cases of lymphadenoma of which I have notes was that of a young man who came to St. Bartholomew's Hospital under Mr. Willett. I incised some tuberculous glands in the neck. He soon died with pulmonary œdema and bilateral hydrothorax. The heart and large vessels were enclosed in one mass of lymphadenoma and there were also masses in the abdomen. Besides the difficulty as to glands, it is easy to confuse lymphadenomatous masses in the lung with tubercle surrounded by hepatisation. The masses in the spleen, sometimes compared to suet in a pudding or to the almonds in toffee ("hardbake"), are due sometimes to lymphadenoma, sometimes to tubercle. Cases by Dietrich,[41] Fischer,[42] Cordua,[43] Ricker,[44] Brentano and Tangle,[45] Tooth,[46] Macnamara,[47] and Dickinson,[48] in addition to many writers already named, afford abundant evidence of the frequency with which these two effects occur together and of the difficulty in distinguishing them. The recent epidemics of influenza, besides causing tuberculosis, have in a number of cases started generalised lymphadenoma.

---

[40] Reinländer: Veterinary Journal, 1892, vol. xxxiv., p. 279.

[41] Dietrich: Beiträge zur Chirurgie von Bruns, 1896, Band xvi., 377.

[42] Fischer: Deutsche Zeitschrift für Chirurgie, 1893, Band xxxvi., 283.

[43] Cordua: Arbeiten an dem Pathologischen Institut zu Göttingen, 1893, S. 159.

[44] Ricker: Archiv für Klinische Chirurgie, 1895, Band i., 573.

[45] Brentano und Tangle: Deutsche Medicinische Wochenschrift, 1891, S. 588.

[46] Tooth: Transactions of the Pathological Society, 1885, vol. xxxvi., p. 236.

[47] Macnamara: Ibid., 1878, vol. xxix., p. 360.

[48] Dickinson: Ibid., 1878, vol. xxix., p. 373.

Lymphadenoma and syphilis.—The connexion is at any rate only an indirect one. Lymphadenoma has frequently started from a chronic, indolent, enlarged gland in the groin which may have been due to previous venereal infection. Again, where generalised lymphadenoma appears in a patient who has suffered from syphilis it may be thought that the latter has predisposed to the former (Guttman).[49] The success of the local application or internal administration of iodine or iodide of potassium cannot be held to indicate the syphilitic origin of the enlarged glands. Wunderlich saw masses of enlarged glands which he regarded as lymphadenoma disappear under iodide treatment in cases in which, he said, syphilis could be excluded. Hutchinson,[50] after describing the disappearance of large masses of glands, did not attribute the good effect of the iodide to the fact that syphilis was the cause of the enlargement, but said that it was interesting that any form of lymphadenoma should yield so readily to the iodide treatment. A woman still under my care had a characteristic mass of lymphadenoma on both sides of the neck which was extremely hard. The disease did not improve under arsenic alone; I then administered iodide internally and applied an iodide ointment externally, and this has been followed by a gradual disappearance of the glands. Before doing so I made an exploratory incision at one place which was exceedingly hard and painful; and in order to exclude tubercle I cut out a piece of tissue, which under the microscope was found to consist of sclerosed gland tissue with thick-walled vessels.

Lymphadenoma and its treatment by arsenic.—It is well known that arsenic is a most valuable drug in the treatment of lymphadenoid diseases, so that the benign and the malignant forms are often distinguished by the success or failure of the arsenical treatment. But the success or failure of the drug depends upon circumstances. The treatment must begin before complications have arisen; large doses are generally required. One preparation of arsenic will act better on, and be better borne by, one patient than another. Katzenstein[51] has described his success in "leukæmia lymphatica et splenica," accompanied by anæmia and cachexia, to the subcutaneous administration of arsenic. Liquor arsenicalis may be injected into the back or directly into the tumour. Touton[52] has described a case of general

---

[49] Guttman: Centralblatt für die Medicinische Wissenschaften, 1895, S. 336.

[50] Hutchinson: Archives I., 72; II., 204.

[51] Katzenstein: Deutsches Archiv für Klinische Medicin, 1895. Band lvi., S. 121.

[52] Touton: Sitzungsberichte der Gesellschaft für Morphologie und Physiologie, München, 1893, Band viii., S. 86.

"sarcoma of the skin of leukæmic or pseudo-lukæmic origin" which was cured by arsenic. In Butlin's[53] case there was a bilateral affection of the testicle with nodules in the skin. The growths subsided under arsenical treatment. I saw a woman in St. Bartholomew's Hospital under Mr. Willett who had had both breasts removed in the country for malignant disease. The axillæ and infra-clavicular fossæ were one mass of enlarged glands. The whole subsided under arsenic, and presumably, therefore, the tumours of the breast would have done the same. I have already referred to a case in which arsenic was successfully administered after the growth had been partly removed. One should not adhere to the surgical rule which obtains in carcinoma and sarcoma, that removal is only permissible when all the disease can be taken away. Partial removal followed by drug treatment is attended by success and prevents the disease from becoming generalised.

CONCLUSION.

I have noted in the course of these lectures some of the chief features exhibited by diseases of lymphadenoid structures; we may with confidence look forward to an increase before long of our knowledge, especially in two directions. Besides the organisms to which I have already referred to as known causes of lymphadenoid disease many observers have found organisms in lymphadenomatous growths. The results are not yet sufficiently in agreement for any opinion to be formed at present; the organism most frequently seen has been the staphylococcus aureus. There are a number of clinical observations on the effect of administering materials obtained from the thymus, spleen, and bone marrow, and some have been successful. With a greater knowledge of the infection we shall be better able to estimate individual differences in resistance and so obtain more light on the varieties of generalised lymphadenoma. Meanwhile we must base our treatment on the closely allied conditions produced by tubercle and syphilis. Excision of the disease where the conditions are favourable, and the administration both locally and internally of arsenic and iodide in full doses, will be attended by success when undertaken at an early stage, except against the most malignant cases. The treatment of the anæmia is the other important point, and is worthy of more relative attention than the leucocythæmia. Thus an improvement has followed upon the administration of oxygen[54] in cases of lymphadenoma, the diminished number of red cells being assisted in exchanging carbonic acid for oxygen by the large supply of the latter.

---

[53] Quoted by Shattock Brit. Med. Jour., vol. i. 1896, p. 136.
[54] Taylor: Transactions of the Clinical Society, 1895, vol. xxviii., p. 47.

PRINTED AT THE LANCET OFFICE, 423, STRAND, W.C.